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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,198	03/10/2004	Michael J. Munchhof	PC23318A	6197

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PFIZER INC.  
PATENT DEPARTMENT, MS8260-1611  
EASTERN POINT ROAD  
GROTON, CT 06340

EXAMINER

TUCKER, ZACHARY C

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 08/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/798,198

**Applicant(s)**

MUNCHHOF, MICHAEL J.

**Examiner**

Zachary C. Tucker

**Art Unit**

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 5-14 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 19 is/are allowed.
- 6) ☒ Claim(s) 1-4, 15-18 and 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Response to Amendment***

As requested by applicant's counsel in the correspondence filed 12 July 2006 (hereinafter "present amendment"), which is in reply to the Office action mailed 12 April 2006 (hereinafter "previous Office action"), claims 1, 5 and 15 have been amended, new claim 20 has been added.

***Election/Restrictions***

Upon receipt of the present amendment, the examiner has continued the search of the prior art, said search being based on the election of the compound 3-amino-6-phenyl-pyrazin-2-carboxylic acid benzyl amide from the disclosure. The present amendment overcomes rejections based on prior art cited in the previous Office action, so the search of claims which read on the elected species for examination has been expanded. Claims 1-4 still have not been completely searched (compounds wherein R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocycle or heteroaryl), as the continued, expanded search was stopped because prior art anticipating the invention was found. Newly added claim 20 also has not been completely searched (compounds wherein R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocycle or heteroaryl). Claims 5-11 remain withdrawn from consideration as not being readable on the elected species; claims 12-14 remain withdrawn from consideration as being drawn to the nonelected invention.

***Status of Claim Rejections - 35 USC § 112***

In the previous Office action, claims 1-4 and 15-19 were rejected under both the first and second paragraphs of 35 U.S.C. 112, for failing to comply with the enablement requirement insofar as the prodrugs and solvates of the claimed compounds were

specified, and for indefiniteness of the terms "prodrug," "amide," "heterocycloalkyl," "sulfonyl" and "keto."

Claim 19, since it is an independent claim (and was when the previous Office action was prepared), was improperly included in the rejections under this statute, as it does not incorporate limitations of any other pending claim.

The present amendment has remedied all of the deficiencies upon which the rejections under 35 U.S.C. 112 were based. "Prodrug" and "solvate" have been deleted from the claims, and "heterocycloalkyl" has been replaced with "heterocyclyl," which is defined satisfactorily in the specification; "amide" has been deleted, while "sulfonyl" and "keto" have been replaced with partial structural formulae more clearly defining them.

Thus, all rejections previously set forth under 35 U.S.C. 112 have been withdrawn.

#### ***Claim Rejections - 35 USC § 102***

In the previous Office action, claims 1-4 were rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/48152 (Bakthavatchalam et al) and also by De Meester et al, *Journal of Heterocyclic Chemistry*, vol. 24, pages 1109-1116 (July-August 1987).

By virtue of the present amendment, "amino" has been struck from the definition of R<sup>2</sup> while (C<sub>1</sub>-C<sub>8</sub>)alkyl has been changed to (C<sub>6</sub>-C<sub>8</sub>)alkyl and (C<sub>1</sub>-C<sub>8</sub>)alcohol has been changed to (C<sub>6</sub>-C<sub>8</sub>)alcohol. These amendments differentiate the compounds according to the instant claims from Bakthavatchalam et al and De Meester et al, and therefore the rejections under 35 U.S.C. 102, based on those two references, are hereby withdrawn.

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***New Claim Rejections - 35 USC § 112***

Upon review of the claims, the following new rejection under 35 U.S.C. 112, second paragraph, is seen as necessary.

Claims 1-4, 15-18 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 15, 17 and 20, the phrase “substituted or unsubstituted” is recited as a modifier to the alternative identities in the definition of variable  $R^2$ . While it is clear what is contemplated by the term “unsubstituted,” “unsubstituted” is not defined in the specification so as to provide for a clear and concise definition pointing out exactly what applicant intends the term to signify. Specifically, what is not defined is the particular group of substituents from which the optional substitution may be chosen. At page 6 of the instant specification, lines 12-24, an exemplary list of suitable substituents is provided, but this list ends with “and the like,” and begins with “substituents include, but are not limited to.” So, the list of substituents provided by applicant in the specification does not actually limit the term when recited in the claims to any specific meaning. As such, what constitutes “substituted” in the context of the invention is not defined, resulting in claims of indeterminate metes and bounds.

An amendment introducing language in claim 1 and 20 which limits the substituents to a particular group would overcome this rejection. Applicant is cautioned, however, that recitation of the aforementioned list *verbatim* from the specification in a “wherein” clause at the end of claims 1 and 20 will introduce indefiniteness into the

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claims, because the terms “ester” and “ether” (appearing in line 20 of page 6) are compounds *per se*, *not* substituents. Striking “ester” and “ether” from the list appearing on page 6 of the instant specification, and amending claims 1 and 20 to specify “wherein ‘substituted’ refers to one or more substitutions with a substituent selected from the group consisting of...” is recommended.

In claims 1 and 20, in the definition of  $R^2$ , the terms “(C<sub>6</sub>-C<sub>8</sub>)alcohol” and “(C<sub>1</sub>-C<sub>8</sub>)alcohol,” respectively, are recited. An alcohol is a compound *per se*, not a substituting moiety on a molecule. “Alcohol” is not standard chemical terminology for describing a substituent. If what applicant intends by the term is a hydroxy-substituted alkyl group, then the claims should recite as much. “Alcohol” is indefinite not only because it is not standard terminology for describing a substituent on a molecule, but because, even if it is assumed that what is being referred to is a hydroxy-alkyl group, the term “alcohol” is ambiguous because it does not specify where the hydroxy-alkyl group is bonded – it could be bonded to the rest of the molecule through the oxygen atom, which would provide an alkoxy group, or through one of the carbon atoms, which would provide a hydroxy-alkyl group. Applicant is urged to amend “(C<sub>6</sub>-C<sub>8</sub>)alcohol” and “(C<sub>1</sub>-C<sub>8</sub>)alcohol” to “(C<sub>6</sub>-C<sub>8</sub>)hydroxyalkyl” and “(C<sub>1</sub>-C<sub>8</sub>)hydroxyalkyl,” respectively. It is important that corresponding changes be made wherever the term “(C<sub>1</sub>-C<sub>8</sub>)alcohol” is recited in the specification, else the amendment to the claims will not have support therein. It is an obvious typographical error being corrected, so the amendment to the specification and claims suggested in the preceding will not constitute new matter. The examples also provide for support – hydroxyalkyl groups are clearly shown in  $R^2$  of

many of the disclosed compounds. In the instant specification, the term “(C<sub>1</sub>-C<sub>8</sub>)alcohol” is found at page 1, line 21; page 2, lines 10, 24 and 25; page 3, line 1.

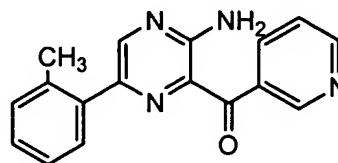
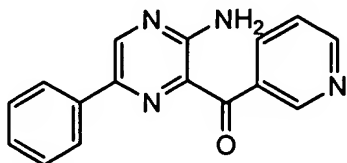
Claim 20 is further indefinite, in addition to reasons set forth above, because the exclusionary proviso lacks antecedent basis in the claim. The compound excluded by the proviso's language is not possible from the formula (I) in claim 20, for at least the reason that n must equal at least 1. The phenyl ring at the 6-position on the central pyrazine ring of the compound cannot be unsubstituted when n must equal at least one, so the compound recited in the proviso, wherein an unsubstituted phenyl ring is at the 6-position, is not possible from the formula.

All claims 2-4, 15-18 are rejected as indefinite, because all depend either directly or indirectly from an indefinite base claim.

***New Claim Rejections - 35 USC § 102***

Claims 1-4 and 20 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by WO 03/004475 (Berg et al). The document is cited in the Information Disclosure Statement filed in the instant application 18 June 2004. Berg et al is prior art under 35 U.S.C. 102(e) because the international filing date is after 29 November 2000, it designates the United States (see section 81 on the cover page) and is published in the English language. The international filing date of the publication is 3 July 2002, before the effective U.S. filing date of the instant application, and the publication date of the Berg et al reference is 16 January 2003, before the effective U.S. filing date of the instant application.

At page 26 of Berg et al, the compounds 3-amino-6-phenyl-N-(pyridin-3-yl)-pyrazine-2-carboxamide and 3-amino-6-(2-methylphenyl)-N-(pyridin-3-yl)-pyrazine-2-carboxamide are disclosed. The structure diagrams shown below represent these compounds:



The first named compound anticipates claims 1-4 wherein  $R^2$  is  $(C_3-C_9)$ heteroaryl – pyridyl and  $n=0$  while  $R^3$  is H, bromo, chloro, cyano, methoxy,  $(C_1-C_8)$ alkyl-SO<sub>2</sub>- or  $(C_1-C_8)$ alkylC(=O)-. The second compounds anticipates all claims 1-4 and 20 wherein  $R^2$  is  $(C_3-C_9)$ heteroaryl – pyridyl and  $n=1$ , wherein  $R^3$  is  $(C_1-C_8)$ alkyl – methyl.

#### ***Allowable Subject Matter***

Claims 15-18 would be allowable if the new rejections under 35 U.S.C. 112, second paragraph, are overcome. Applicant is urged to amend as suggested in the section hereinabove headed "New Claim Rejections - 35 USC § 112." The closest prior art with respect to the compounds according to claims 15-18 is the De Meester and Bakthavatchalam et al references cited in the previous Office action, and the Berg et al publication cited in this Office action (and also in applicant's Information Disclosure Statement).

Claim 19 is allowed.

Claims 12-14 will be rejoined upon receipt of an amendment placing claims 1-4, 15-18 and 20 in allowable form. At such time, it would be necessary to reject claims 13 and 14 under 35 U.S.C. 112, for lack of enablement of the claimed methods, and also



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for indefiniteness, as all TGF-related disease states are not known or understood, nor have all such diseases been discovered. The lack of any showing of biological activity in the instant specification speaks to the lack of a disclosure enabling one of ordinary skill in the art to practice the claimed method of treating and preventing, for example, all cancers (treatment and prevention of "cancer," generally, is recited in claim 14). Cancellation of claims 13 and 14 is recommended, to allow the case to pass to issue forthwith.

#### ***Abstract of the Disclosure***

Objection to the abstract of the disclosure was set forth in the previous Office action, page 16. Applicant's counsel has not addressed the objection to the abstract. It is requested that applicant amend the abstract so that the generic structure of the compounds according to claim 1 be incorporated therein, to more fully and accurately describe the invention disclosed.

#### ***Conclusion***

Were it not for the new rejections under 35 U.S.C. 112, second paragraph, which are set forth in this Office action, it would have been made final. A rejection based on newly cited prior art may serve as grounds for issuing a Final Rejection of a patent application, when an election of species requirement is operative, as is the case with the instant application (MPEP 803.02 "Markush Practice"). The indefiniteness rejection newly set forth should have been made in the previous Office action, however.

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 5:45am to 2:15pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

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The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

zt

A handwritten signature in black ink, appearing to be "Z. L. H.", followed by a long horizontal line.